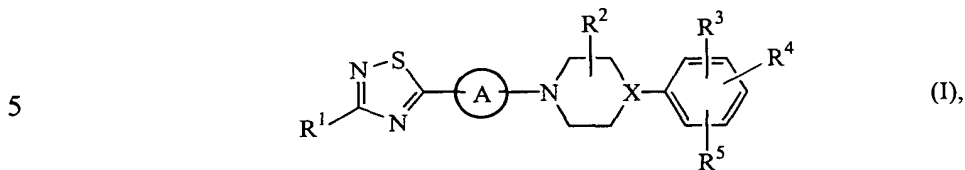


-17-

Claims

1. A compound of formula (I),



the *N*-oxide forms, the pharmaceutically acceptable acid addition salts and stereochemically isomeric forms thereof, wherein

X is CH or N;

10 R^1 is hydrogen, C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} alkylthio, amino, mono- or di(C_{1-6} alkyl)amino, Ar^1 , Ar^1NH- , C_{3-6} cycloalkyl, hydroxymethyl or benzyloxymethyl;

R^2 is hydrogen, C_{1-6} alkyl, amino, aminocarbonyl, mono- or di(C_{1-6} alkyl)amino, C_{1-6} alkyloxycarbonyl, C_{1-6} alkylcarbonylamino, hydroxy or C_{1-6} alkyloxy;

15 R^3 , R^4 and R^5 are each independently selected from hydrogen, halo, C_{1-6} alkyl, C_{1-6} alkyloxy, trifluoromethyl, nitro, amino, cyano, azido, C_{1-6} alkyloxy C_{1-6} alkyl, C_{1-6} alkylthio, C_{1-6} alkyloxycarbonyl or Het^1 ;
 —(A)— is Ar^2 , Ar^2CH_2- or Het^2 ;

20 Ar^1 is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy, trihalomethyl, amino or nitro;

Ar^2 is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C_{1-6} alkyl, C_{1-6} alkyloxy, trihalomethyl, amino or nitro;

25 Het^1 is a monocyclic heterocycle selected from oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl or oxazoliny; and each monocyclic heterocycle may optionally be substituted on a carbon atom with C_{1-4} alkyl; and

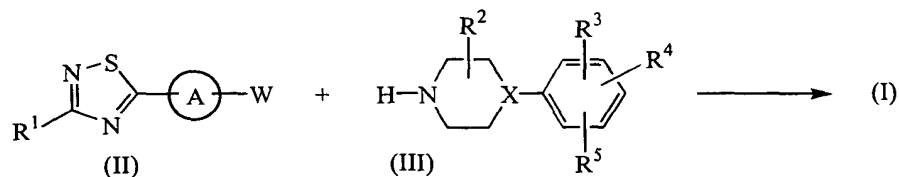
30 Het^2 is a monocyclic heterocycle selected from furanyl, thiofuranyl, oxadiazolyl, thiadiazolyl, pyridinyl, pyrimidinyl or pyrazinyl; and each monocyclic heterocycle may optionally be substituted on a carbon atom with 1 or 2 substituents each independently selected from halo, C_{1-4} alkyl, C_{1-4} alkyloxy, nitro or trifluoromethyl.

-18-

2. A compound according to claim 1 wherein X is N; R¹ is hydrogen, C₁₋₆alkyl, amino or di(C₁₋₆alkyl)amino; R² is hydrogen; R³, R⁴ and R⁵ are each independently selected from hydrogen, halo, C₁₋₆alkyl, C₁₋₆alkyloxy, trifluoromethyl, nitro or C₁₋₆alkyloxycarbonyl.
- 5
3. A compound according to any of claims 1 or 2 wherein X is N; R¹ is hydrogen, C₁₋₄alkyl or di(C₁₋₄alkyl)amino; R² is hydrogen; R³, R⁴ and R⁵ are each independently selected from hydrogen, halo, C₁₋₄alkyl, C₁₋₄alkyloxy or trifluoromethyl; and the bivalent radical $\text{---}(\text{A})\text{---}$ is Ar², Ar²CH₂- or Het²
- 10 wherein Ar² is phenyl and Het² is thiadiazolyl, pyridinyl, pyrimidinyl or pyrazinyl..
4. A compound according to any of claims 1 to 3 wherein X is N, R¹ is methyl, R² is hydrogen, R³ and R⁴ are hydrogen and R⁵ is trifluoromethyl
- 15
5. A compound according to claim 1 wherein the compound is
1-[4-(3-methyl-1,2,4-thiadiazol-5-yl)phenyl]-4-[3-(trifluoromethyl)phenyl]-
piperazine; or
1-[5-(3-methyl-1,2,4-thiadiazol-5-yl)-2-pyridinyl]-4-[3-(trifluoromethyl)phenyl]-
20 piperazine; a stereoisomeric form or a pharmaceutically acceptable acid addition
salt thereof.
6. A composition comprising a pharmaceutically acceptable carrier, and as active
ingredient a therapeutically effective amount of a compound as claimed in any one
25 of claims 1 to 5.
7. A process of preparing a pharmaceutical composition as claimed in claim 6
wherein the pharmaceutically acceptable carriers and a compound as claimed in
claim 1 to 5 are intimately mixed.
- 30
8. A compound as claimed in any one of claims 1 to 5 for use as a medicine.
9. Use of a compound as claimed in any one of claims 1 to 5 for the manufacture of a
medicament for the treatment of angiogenesis dependent disorders.
- 35
10. A process of preparing a compound as claimed in claim 1, wherein

-19-

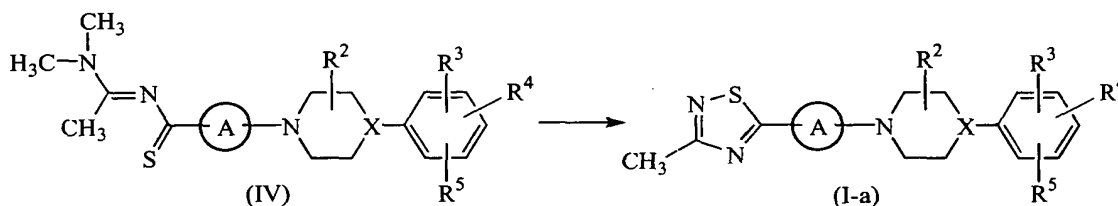
- a) an intermediate of formula (II) is reacted with an intermediate of formula (III) in a reaction-inert solvent and, optionally in the presence of a suitable base;



5

- b) an intermediate of formula (IV) is treated with hydroxylamino-O-sulfonic acid in a reaction-inert solvent, in the presence of a suitable base, thereby yielding compounds of formula (I-a), defined as compounds of formula (I) wherein R¹ is methyl;

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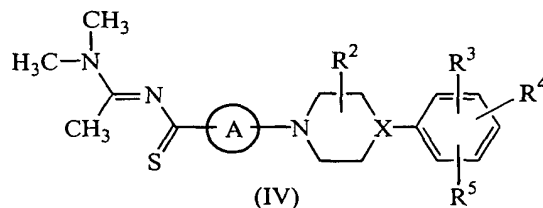
wherein in the above reaction schemes the radicals X, R¹, R², R³, R⁴, R⁵ and $\text{---}(\text{A})\text{---}$ are as defined in claim 1, and W is an appropriate leaving group;

15

- c) or, compounds of formula (I) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

20

11. A compound of formula (IV),

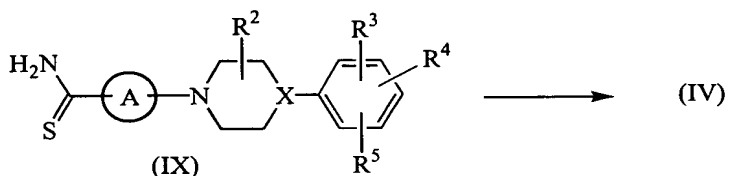


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-20-

an acid addition salt, a *N*-oxide form or a stereochemically isomeric form thereof, wherein X, R², R³, R⁴, R⁵ and the bivalent radical $\text{---}(\text{A})\text{---}$ are as defined in claim 1.

- 5 12. A process of preparing a compound of formula (IV) as claimed in claim 10, wherein
- a) an intermediate of formula (IX) is treated with *N,N*-dimethylacetamide dimethyl acetal in a reaction-inert solvent, thereby yielding a compound of formula (IV);



- 15 b) or, compounds of formula (IV) are converted into each other following art-known transformation reactions; or if desired; a compound of formula (IV) is converted into an acid addition salt, or conversely, an acid addition salt of a compound of formula (IV) is converted into a free base form with alkali; and, if desired, preparing stereochemically isomeric forms thereof.